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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
10/789,807	02/27/2004	Benjamin Tjoa	020093-003710US	5631
20350 75	590 08/23/2006		EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER			JUEDES, AMY E	
EIGHTH FLOO			ART UNIT	PAPER NUMBER
SAN FRANCIS	SCO, CA 94111-3834		1644	
			DATE MAILED: 08/23/2006	;

Please find below and/or attached an Office communication concerning this application or proceeding.

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	Application No.	Applicant(s)
	10/789,807	TJOA ET AL.
Office Action Summary	Examiner	Art Unit
	Amy E. Juedes, Ph.D.	1644
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DATE of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication. If NO period for reply is specified above, the maximum statutory period was reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be tin will apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONE	N. nely filed the mailing date of this communication. D (35 U.S.C. § 133).
Status		
1)⊠ Responsive to communication(s) filed on <u>19 Ju</u> 2a)⊡ This action is FINAL . 2b)⊠ This	<u>une 2006</u> . action is non-final.	
3) Since this application is in condition for allowar closed in accordance with the practice under E	•	
Disposition of Claims		
4) ☐ Claim(s) 1 and 3-29 is/are pending in the application 4a) Of the above claim(s) 4-7,10-12,16 and 24-5) ☐ Claim(s) is/are allowed. 6) ☐ Claim(s) 1, 3, 8-9, 13-15, 17-18, 21-23 is/are reference objected to. 8) ☐ Claim(s) are subject to restriction and/or	. <u>29</u> is/are withdrawn from conside	eration.
Application Papers		
9) The specification is objected to by the Examine 10) The drawing(s) filed on is/are: a) accomplicant may not request that any objection to the Replacement drawing sheet(s) including the correct 11) The oath or declaration is objected to by the Examine	epted or b) objected to by the drawing(s) be held in abeyance. Section is required if the drawing(s) is object.	e 37 CFR 1.85(a). jected to. See 37 CFR 1.121(d).
Priority under 35 U.S.C. § 119		
12) Acknowledgment is made of a claim for foreign a) All b) Some * c) None of: 1. Certified copies of the priority document: 2. Certified copies of the priority document: 3. Copies of the certified copies of the priority application from the International Bureau * See the attached detailed Office action for a list	s have been received. s have been received in Applicati rity documents have been receive u (PCT Rule 17.2(a)).	on No ed in this National Stage
Attachment(s) 1) Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date	4) Interview Summary Paper No(s)/Mail D 5) Notice of Informal F 6) Other:	

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DETAILED ACTION

1. Applicant's amendment and remarks, filed 6/19/06, are acknowledged.

Claims 3, 18, and 21 have been amended. Claim 2 has been cancelled. Claims 1 and 3-29 are pending.

2. Claims 4-7, 10-12, 16, and 24-29 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1, 3, 8-9, 13-15, and 17-23 are being acted upon.

- 3. The objection for the lack of sequence listing under 37 C.F.R. 1.821 1.825 is withdrawn in view of Applicants submission of the CRF, sequence listing, and statement that the two are identical.
- 4. The objection to the specification for improperly incorporating essential material is withdrawn in view of Applicant's amendment to the specification to include the material.
- 5. The objection to the claims for informalities is withdrawn in view of Applicant's amendment.
- 6. The specification stands objected to for the use of trademarks (e.g. $TEFLON^{TM}$, on pg. 11 and $PLASBUMIN^{TM}$, on page 22). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.
- 7. Upon reconsideration, the rejections of the claims under 112 first and second paragraph are withdrawn.
- 8. The rejection of the claims as being obvious over Sallusto and U.S. Patent Application publication 2005/0173315 is withdrawn in view of Applicant's statement that the applications were commonly owned at the time the claimed invention was made.

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9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 14, 19, and 23 stand rejected, and claims 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sallusto et al., 1994, J. Exp. Med.

As set forth previously, Sallusto teaches a method for generating dendritic cells from peripheral blood mononuclear cells (i.e. monocytic dendritic cell precursors) by culturing in GM-CSF in the absence of additional cytokines (see Table 1). Furthermore, said dendritic cells are immature, as evidenced by their expression of CD11c and MHC, but lack of expression of B7 (see Table 1). Furthermore, the monocytic dendritic cell precursors used to generate the immature dendritic cells were non-activated (i.e. isolated on a Percoll gradient without positive selection or other stimulation- see materials and methods). Additionally, the differentiated dendritic cells were contacted with a bacterial antigen (tetanus toxoid) for a time period sufficient for antigen uptake, as evidence by their ability to stimulate tetanus toxoid specific T cells (see Table 1).

Applicant's arguments filed 6/19/06 have been fully considered, but they are not persuasive.

Applicant argues that the cells cultured in GM-CSF without IL-4 taught by Sallusto are not immature dendritic cells since they lack B7 and CD1a expression.

However, it is noted that the instant claims are not limited to an immature dendritic cell that expresses CD1a or B7.

Applicant further argues that Sallusto states that the DC lines require IL-4 in addition to GM-CSF to maintain their immature state.

However, it is noted that the instant method is a method of differentiating immature dendritic cells, and not a method of maintaining immature dendritic cells. Furthermore, Applicant's arguments are not persuasive since Sallusto have performed the exact steps of the instantly claimed method and therefore must have inherently obtained an immature dendritic cell.

It is noted that claims 17-18 have been included as being anticipated by Sallusto et al. The instant method is drawn to a

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method for differentiating monocytic precursors and not to a method of enriching precursors. Therefore, the manner in which the precursors are obtained does not carry any patentable weight in the absence of as structural difference. It is the Examiner's position that precursors enriched by tangential flow filtration would be the same as the precursors of Sallusto et al.

- 10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
- 11. Claims 3 and 8-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sallusto et al., 1994, J. Exp. Med, in view of Bernard et al., 1998, Hem. Cell. Ther.

As set forth previously, The teachings of Sallusto are described above.

Sallusto does not culture in a low avidity culture vessel comprising PFTE.

Bernard teaches a method to generate dendritic cells from purified blood monocytes by culturing in a $\text{TEFLON}^{\text{tm}}$ (i.e. comprising PFTE) bag. Furthermore, Bernard teaches that said method meets good laboratory practice (GLP) procedures necessary for the clinical use of dendritic cells (see pg. 23).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an immature dendritic cell, as taught by Sallusto, using the TEFLONtm culture vessel, as taught by Bernard. The ordinary artisan at the time the invention was made would have been motivated to do so, since Bernard teaches that this method is useful for clinical purposes, since it involves the large scale differentiation of dendritic cells in a culture system that meets GLP procedures (see abstract and pg. 23). Moreover, one of ordinary skill in the art would have a reasonable expectation of success.

Applicant's arguments filed 6/19/06 have been fully considered, but they are not persuasive.

Applicant argues that the cells taught by Sallusto are not "immature dendritic cells", as recited in the instant claims.

However, as noted above, Sallusto et al. have performed the exact steps of the claimed method, and therefore must have obtained immature dendritic cells.

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11. Claim 13 and 20-22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sallusto et al., 1994, J. Exp. Med, in view of Bosch et al., 2001, J. Invest. Derm., meeting abstract.

As set forth previously, the teachings of Sallusto are described above.

Sallusto does not teach generating immature dendritic cells in serum free medium, nor maturing dendritic cells with IFN-yand BCG.

Bosch teaches that dendritic cells can be successfully generated in serum free medium, and that dendritic cells can be matured with a combination of INF-and BCG. Furthermore, Bosch teaches that dendritic cells are extremely useful for therapeutic purposes, and that the serum free culture medium (in contrast to the FBS containing medium taught by Sallusto) complies with the good manufacturing practice conditions that are required for clinical trials. Additionally, Bosch teaches that maturation with IFN- γ and BCG results in a dendritic cell population that can induce a immune response against a tumor antigen in cancer patients (i.e. a therapeutically useful dendritic cell population).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make an immature dendritic cell, as taught by Sallusto, using serum free medium, as taught by Bosch. The ordinary artisan at the time the invention was made would have been motivated to use serum free medium, since Bosch teaches that dendritic cells are extremely useful for therapeutic purposes, and that the serum free culture medium (in contrast to the FBS containing medium taught by Sallusto) complies with the good manufacturing practice conditions that are required for clinical trials. Furthermore, it would have been obvious to one of ordinary skill in the art to mature the dendritic cells, as taught by Sallusto, with BCG and IFN-γas taught by Bosch. The ordinary artisan would have been motivated to do so, since Bosch teaches that IFN-yand BCG are extremely potent maturation agents that result in a dendritic cell population that can induce a immune response against a tumor antigen in cancer patients (i.e. a therapeutically useful dendritic cell population). Moreover, one of ordinary skill in the art would have a reasonable expectation of success, since Bosch teaches the effectiveness of these techniques in the generation of dendritic cells.

Applicant's arguments filed 6/19/06 have been fully considered, but they are not persuasive.

Applicant argues that the cells taught by Sallusto are not "immature dendritic cells", as recited in the instant claims.

However, as noted above, Sallusto et al. have performed the exact steps of the claimed method, and therefore must have obtained immature dendritic cells.

12. Claim 15 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Sallusto et al., 1994, J. Exp. Med, in view of Lewalle et al., 2000, J. Immunol. Methods.

As set forth previously, The teachings of Sallusto are described above.

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Sallusto does not teach using a cryopreserved cell population to generate dendritic cells.

Lewalle teaches the generation of dendritic cells from frozen peripheral blood mononuclear cells (see pg. 70). Furthermore, Lewalle teaches that many clinical protocols are based on sequential injections of dendritic cells, and therefore it would be of practical importance to have frozen aliquots of the same peripheral blood mononuclear cells for these purposes (see pg. 70).

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Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an immature dendritic cell, as taught by Sallusto, using frozen peripheral blood mononuclear cells, as taught by Lewalle. The ordinary artisan at the time the invention was made would have been motivated to do so, since Lewalle teaches that many clinical protocols are based on sequential injections of dendritic cells (see pg. 70), and therefore it would be of practical importance to have frozen aliquots of the same peripheral blood mononuclear cells for these purposes.

Furthermore, the ordinary artisan would have had a reasonable expectation of success, since Lewalle teaches that dendritic cells derived from frozen peripheral blood mononuclear cells retain their functional capacity (see pg. 73).

Applicant's arguments filed 6/19/06 have been fully considered, but they are not persuasive.

Applicant argues that the cells taught by Sallusto are not "immature dendritic cells", as recited in the instant claims.

However, as noted above, Sallusto et al. have performed the exact steps of the claimed method, and therefore must have obtained immature dendritic cells.

- 13. No claim is allowed.
- 14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amy E. Juedes, Ph.D. Patent Examiner Technology Center 1600 August 11, 2006

G.R. EWOLDT, PH.D. PRIMARY EXAMINER